# A REVIEW OF SODIUM MONOFLUOROACETATE (COMPOUND 1080)

## Its Properties, Toxicology, and Use In Predator and Rodent Control

UNITED STATES DEPARTMENT OF THE INTERIOR
FISH AND WILDLIFE SERVICE
BUREAU OF SPORT FISHERIES AND WILDLIFE
Special Scientific Report—Wildlife No. 146

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# A REVIEW OF SODIUM MONOFLUOROACETATE (COMPOUND 1080) ITS PROPERTIES, TOXICOLOGY, AND USE IN PREDATOR AND RODENT CONTROL

By

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Division of Wildlife Services
Bureau of Sport Fisheries and Wildlife

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## INTRODUCTION

Since the Second World War sodium monofluoroacetate, or sodium fluoroacetate (Compound 1080), has been a subject of wide research in the United States and elsewhere. Based on this research, it has been approved for animal damage control work by several nations. In the United States sodium monofluoroacetate has been a tool used by the Bureau of Sport Fisheries and Wildlife to control coyote and rodent damage, as well as a tool used by private pest control operators to control commensal rodents. Despite 25 years of worldwide research and practical experience, the use of Compound 1080 is still embroiled in controversy.

The purpose of this monograph is to summarize current information on sodium monofluoroacetate, to review use patterns, and to provide a base for further studies.

## EARLY RESEARCH

Monofluoroacetic acid ($FCH_2COOH$), the shortest chained ω-fluoro-fatty acid, was first prepared synthetically by Swarts in Belgium in 1896. [1] However, the toxic nature of monofluoroacetate compounds was first noted by Schrader in 1934. His work eventually led to the patenting of monofluoroacetic acid salts as rodenticides in Germany prior to the Second World War. Probably due to the tense political conditions in Europe during the 1930's, little of Schrader's work appeared in the literature. It was brought to light after the Second World War by British Intelligence. In the late 1930's a group of Polish scientists, led by Gryszkiewicz-Trochimowski, also carried out extensive research on the toxic properties of monofluoroacetate compounds. These Polish scientists were able to escape to England following the invasion of Poland by Germany, and in 1942 turned over the results of their work to the British government (Peters, 1957; Pattison, 1959). The British, in turn, investigated the toxic properties of monofluoroacetate compounds and results of these studies were sent to the United States together with a request for cooperation in further research.

In 1944, the Fish and Wildlife Service was operating under a grant from the Office of Scientific Research and Development (OSRD) to find or develop new, effective rodenticides. The war had cut the United States off from major sources of red squill, thallium, and strychnine; and replacements for these important rodenticides were desperately needed. In the Spring of 1944, the National Defense Research Committee (NDRC) of OSRD, responsible for much of the war-connected chemical work with toxic materials, supplied the Patuxent Wildlife Research Center with ten potentially suitable chemicals, including sodium monofluoroacetate. On June 8, 1944, Dr. Ray Treichler at the Patuxent Wildlife Research Center began

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[1] The general formula of ω-fluoro-fatty acids is $FCH_2(CH_2)_nCOOH$.

standard rodent toxicity tests on sodium monofluoroacetate. Sodium monofluoroacetate received the laboratory acquisition number 1080; hence the common name 1080, which subsequently was adopted by the Tull Chemical Company.

Since results of initial experiments with laboratory rats were promising, samples of 1080 were shipped to the Denver Wildlife Research Center for testing on additional species. These tests gave further evidence of 1080's value as an animal damage control tool. Following laboratory tests, widespread field studies were undertaken on 1080. These early studies marked the beginning of over 25 years of continuous worldwide research on the entire spectrum of monofluoroacetates.[2]

## OCCURRENCE IN NATURE

Independently of the early research in England and the United States Marais (1944) identified monofluoroacetic acid as the toxicant in the South African plant gifblaar, Dichapetalum cymosum (Hook) Engl., long recognized as a hazard to livestock. Since Marais' discovery monofluoroacetic acid has been identified as the toxic agent in several other poisonous plants: Acacia georginae, F. M. Bailey (Oelrichs and McEwan, 1961), Gastrolobium grandiflorum, F. Mull. (McEwan, 1964), Gastrolobium callistachys, Meissn., and Oxylobium parviflorum, Benth. (McEwan, 1964a), all native to Australia; and rat weed, Palicourea margravii, St. Hill (DeOliveira, 1963), native to Brazil. Monofluoroacetic acid has also been isolated from ratsbane, Dichapetalum toxicarium (Chailletia toxicacia Don), native to West Africa; however, the major toxic agents of this plant are longer chained $\omega$-fluoro-fatty acids containing an even number of carbon atoms (Peters et al., 1960).[3]

Peters and Shorthouse (1964) found no monofluoroacetic acid in grass seedlings grown in a medium containing inorganic fluoride. However, Cheng et al. (1968) showed that soybeans, Glycine max, Merr., can synthesize monofluoroacetic acid when grown in an atmosphere containing a high level of hydrogen fluoride (43 ppb HF, ambient air 0.06 ppb HF) or when grown in a medium containing a high level of sodium fluoride. Lovelace et al. (1968) isolated monofluoroacetic acid from a mixture of forage crops

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[2] Fluoroethanol, monofluoroacetic acid and its esters, salts, amides, halides, and anhydride.

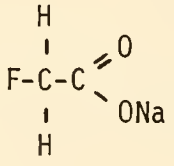
[3] The $\omega$-fluoro-fatty acids containing an odd number of carbon atoms are not toxic. This pronounced alternation in toxicity of $\omega$-fluoro-fatty acids has been correlated with $\beta$-oxidation of fatty acids, a mechanism which yields non-toxic monofluoropropionic acid ($FCH_2CH_2COOH$) from $\omega$-fluoro-fatty acids containing an odd number of carbon atoms, and yields toxic monofluoroacetic acid ($FCH_2COOH$) from $\omega$-fluoro-fatty acids containing an even number of carbon atoms (Pattison, 1959).

including alfalfa, Medicago sativa, L., and crested wheat grass, Agropyron cristatum, (L.) Gearth., growing near a phosphate plant responsible for a high concentration of inorganic fluoride. Preuss (1967) hypothesized that the synthesis of monofluoroacetic acid by plants may perhaps be a metabolic adaptation to the presence of high levels of inorganic fluoride in the environment.

There is a major difference between the results of Cheng et al. (1968) and Lovelace et al. (1968), as compared with the results of investigations on the toxic plants. Both identified fluorocitrate; 140 μg. per gram of dry weight of tissue, and 896 μg. per gram of dry weight of tissue, respectively, a compound not noted in the toxic plants mentioned previously. The significance of this fact will be developed under the section entitled Mode of Action. Additionally, horses grazing the plants in the Lovelace et al. (1968) study area exhibited symptoms of fluoride poisoning, not symptoms of monofluoroacetate poisoning. This indicates that the toxic effect of the inorganic fluoride absorbed by the plant and not incorporated into monofluoroacetic acid was greater than the toxic effect of the amount of monofluoroacetic acid which the plants synthesized (179 μg. per gram of dry weight of tissue).

## PHYSICAL PROPERTIES

Sodium monofluoroacetate is a white, odorless, powdery, fluoro-organic salt similar in appearance to flour, powdered sugar, or baking powder. It is essentially tasteless, having only a mild salty, sour or vinegar taste to some individuals.




Being hygroscopic, it absorbs atmospheric water and becomes somewhat sticky. It is highly soluble in water, but relatively insoluble in organic solvents such as kerosene, alcohol, acetone, or in animal and vegetable fats and oils.

## CHEMICAL PROPERTIES

Monofluoroacetates, in general, are chemically stable due to the strength of the carbon-fluorine bond. However, Chenoweth (1949) and Harrison et al. (1951) reported that sodium monofluoroacetate and some other monofluoroacetate compounds exhibit instability in aqueous solutions, losing a portion of their toxicity over time. This was corroborated by Preuss and Weinstein (1969). Sodium monofluoroacetate is

unstable above 110 degrees centigrade, and decomposes at 200 degrees centigrade (Pesticide Chemicals Official Compendium, 1966) yielding approximately 20 percent hydrogen fluoride by weight (Denver Wildlife Research Center, unpublished data). Hydrogen fluoride, similar in nature to hydrogen chloride, readily reacts with metals or metal compounds to form stable inorganic fluoride compounds.

## ABSORPTION AND DISTRIBUTION

Sodium monofluoroacetate is absorbed through the gastrointestinal tract, open wounds, mucous membranes, and the pulmonary epithelium (Saunders and Stacey, 1948). It is not readily absorbed through intact skin (Pattison, 1959). It appears that sodium monofluoroacetate has substantially the same oral toxicity whether the carrier is water, meat, grain, oil, gum acacia suspension, or gelatin capsule (Denver Wildlife Research Center, unpublished data). Further, the toxicity is approximately the same whether the chemical is administered orally, subcutaneously, intramuscularly, intraperitoneally, or intravenously (Chenoweth and Gilman, 1946; Quin and Clark, 1947).

Gal et al. (1961) administered sodium monofluoro-2-$^{14}$C-acetate intraperitoneally to rats to study the distribution of the radioactivity at death.[4] The rats, all moribund, were sacrificed 4 hours after the administration of the sodium monofluoro-2-$^{14}$C-acetate, and the distribution of the radioactivity was determined (Table 1).

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[4] Sodium monofluoro-2-$^{14}$C-acetate is chemically the same as sodium monofluoroacetate. The presence of the radioactive isotope ($^{14}$C) allows the distribution and metabolic fate of the compound to be determined more easily.

TABLE 1. Distribution of radioactivity 4 hours after intraperitoneal administration to rats as sodium monofluoro-2-$^{14}$C-acetate (10.53 mg/kg) (adapted from Gal et al., 1961).

| Tissue | Wet weight of tissue | Percent of radioactivity found | Concentration of label |
|---|---|---|---|
| | g. | | μg. monofluoro-acetate/g. wet weight* |
| Brain | 1.33 | 2.26 | 26.9 |
| Heart | 0.93 | 1.26 | 21.4 |
| Kidneys | 1.95 | 2.49 | 20.1 |
| Liver | 8.47 | 11.95 | 22.3 |
| Lungs | 8.82 | 4.05 | 16.8 |
| Intestines and Stomach | 9.60 | 10.33 | 17.0 |
| Carcass | 115.00 | 59.70 | 8.2 |
| Testes | 2.50 | 2.28 | 14.4 |
| Spleen | 1.96 | 2.00 | 16.2 |
| Excreted Urine | | 0.50 | |
| Expired $^{14}CO_2$ | | 1.00 | |
| Total | 150.56 | 97.82 | |

* Based on the assumption that none of the sodium monofluoro-2-$^{14}$C-acetate is metabolized.



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## MODE OF ACTION

The toxicity of monofluoroacetates to biological systems is related to the inhibition of citrate metabolism (Peters, 1952) and succinate metabolism (Fanshier et al., 1964) within the citric acid, or Krebs cycle. This cycle is the final mechanism for converting food to energy in plants and animals.[5] The inhibition is caused by fluorocitrate, a metabolite of monofluoroacetic acid (Peters et al., 1953).[6] Peters (1952) coined the term "lethal synthesis" to emphasize that physiologically the actual toxicant is a product of metabolic alterations of monofluoroacetic acid.

The synthesis of fluorocitrate from monofluoroacetic acid is similar to that of citrate from acetic acid. Both acetic and monofluoroacetic acids combine with coenzyme A (CoA) in the presence of adenosine - 5' - triphosphate (ATP) to form acetyl-CoA and fluoroacetyl-CoA, respectively (Goldman, 1969). Acetyl-CoA and fluoroacetyl-CoA then react with oxaloacetate and water in the presence of 'condensing enzyme,' forming citrate and fluorocitrate respectively.[7] However, whereas citrate then continues through the Krebs cycle, fluorocitrate does not.

Fluorocitrate inhibits aconitase,[8] the enzyme responsible for catalyzing citrate metabolism; and inhibits succinate dehydrogenase, the enzyme responsible for catalyzing succinate metabolism. Fluorocitrate inhibits aconitase via two distinct kinetic mechanisms: (a) direct competitive inhibition, and (b) time dependent progressive inhibition. However, fluorocitrate inhibits succinate dehydrogenase only via the former mechanism (Fanshier et al., 1964). Pattison (1959) suggested that the competitive inhibition of aconitase is due to an irreversible combination of fluorocitrate with aconitase.

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[5] Plants are much less sensitive to sodium monofluoroacetate than are animals (David and Gardiner, 1951).

[6] Esters, salts, amides, acid halides, and the acid anhydride of monofluoroacetic acid all exhibit toxic action on the basis of their first being hydrolized in vivo to the parent acid. The differential toxic action among these compounds is due in part to the rate and degree to which each is hydrolyzed to the parent acid in vivo (Pattison, 1959).

[7] In view of the similar size of the fluorine atom (Van der Waals' radius 1.35 angstroms) and the hydrogen atom (Van der Waals' radius 1.1 angstroms), it is not surprising that an enzyme can catalyze reactions of both acetyl-CoA and fluoroacetyl-CoA (Goldman, 1969).

[8] Only one of the four isomers of fluorocitrate inhibits aconitase, that being the isomer formed enzymatically from fluoroacetyl-CoA and oxaloacetate (Fanshier et al., 1964).

The inhibition of these two enzymes blocks the Krebs cycle. The resulting increase of citrate secondarily blocks glucose metabolism, a lesser energy producing process, by inhibiting phosphofructokinase (Dunn and Berman, 1966). The blockage of these processes causes the energy supply to be reduced to a point where cellular permeability barriers are destroyed, resulting in loss of function and finally cellular death.

## TOXICOLOGY

Eventually the breakdown in intracellular processes caused by fluorocitrate results in the appearance of gross organ or organ system disorders. Death may result from: (a) gradual cardiac failure or ventricular fibrillation; or (b) progressive depression of the central nervous system with either cardiac or respiratory failure as the terminal event; or (c) respiratory arrest following severe convulsions. In general, death in herbivorous species is the result of cardiac disorders and in carnivorous species the result of central nervous system disorders. Death in omnivorous species tends to result from disorders of both the heart and central nervous system (Chenoweth, 1949). In general, cold-blooded vertebrates are less sensitive to sodium monofluoroacetate than are warm-blooded vertebrates. Table 2 gives the $LD_{50}$'s for numerous species.[9] Table 3 gives the amount of properly treated coyote bait (1.6 g. 1080 per 45.4 kg. of bait material) that selected species must consume in order to obtain a median lethal dose.

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[9] The $LD_{50}$ (median lethal dosage) is a statistical estimate of the dosage that would be lethal to 50 percent of a very large population of a species.

TABLE 2. $LD_{50}$'s of sodium monofluoroacetate.

| Species | $LD_{50}$* mg/kg | 95% Confidence Interval | Route of Administration | Reference |
|---|---|---|---|---|
| MAMMALS | | | | |
| Primates | | | | |
| Man | 0.7-2.1 | Estimated | Oral | 1,2 |
| Rhesus monkey (Macaca mulatta) | 4.0 | | I.V. | 3 |
| Spider monkey (Ateles geoffroyi) | 15.0 | | I.V. | 3 |
| Marsupials | | | | |
| Opossum (Didelphis marsupialis) | 60.0 | | Oral | 9 |
| Ungulates | | | | |
| Cow | | | | |
| adults(F) | 0.393 | 0.247-0.625 | Oral | 4 |
| juvenile (M-F) | 0.221 | 0.149-0.327 | Oral | 4 |
| Goat | 0.6 | | I.M. | 3 |
| Horse (M-F) | 0.35-0.55 | | Oral | 5 |
| Mule (M-F) | 0.22-0.44 | | Oral | 5 |
| Mule Deer (Odocoileus h. hemionus) M-F | 0.30-1.00 | | Oral | 5 |
| Sheep (M-F) | 0.25-0.50 | | Oral | 6 |
| Swine | | | | |
| adult | < 1.0 | | Oral | 3 |
| young | 0.4 | | Oral | 3 |
| Carnivores | | | | |
| Bear (Ursus sp.) | 0.5-1.0 | | Oral | 7 |

TABLE 2--continued

| Species | $LD_{50}$* mg/kg | 95% Confidence Interval | Route of Administration | Reference |
|---|---|---|---|---|
| Bobcat (Lynx rufus baileyi) | < 0.66 | | I.P. | 8 |
| Domestic cat | 0.20 | | I.V. | 8 |
| Coyote (Canis latrans nebracensis) | 0.10 | | I.V. | 8 |
| Grey Fox (Urocyon cinereoargenteus scotti) | < 0.3 | | I.P. | 8 |
| Badger (Taxidea taxus berlandieri) | 1.0-1.5 | | I.P. | 8 |
| Domestic ferret (Mustela putorious) | 1.41 | | Oral (S.T.) | 5 |
| Marten (Martes americana) | ~ 1.0 | | Oral | 7 |
| Mink (Mustela vison) | ~ 1.0 | | Oral | 7 |
| Rodents | | | | |
| Ground Squirrels: | | | | |
| Columbia (Citellus c. columbianus) | 0.9 | | I.P. | 3 |
| Fisher's (Citellus beecheyi fisheri | 0.3 | | Oral | 3 |
| Pocket Gophers: | | | | |
| Breviceps (Geomys breviceps sp.) | < 0.05 | | I.P. | 3 |
| Tuza (Geomys floridanus) | 0.2 | | I.P. | 3 |

TABLE 2--continued

| Species | $LD_{50}$* mg/kg | 95% Confidence Interval | Route of Administration | Reference |
|---|---|---|---|---|
| Kangaroo Rats: | | | | |
| Bannertail (Dipodomys s. spectabilis) | 0.1 | | I.P. | 8 |
| Merriam (Dipodomys m. merriami) | 0.15 | | I.P. | 3 |
| Rats: | | | | |
| Norway-lab (Rattus norvegicus) M | 2.1** | | Oral | 9 |
| F | 2.2** | | Oral | 9 |
| Alexandrine (Rattus rattus alexandricus) | 0.5 | | Oral | 3 |
| Black (Rattus rattus sp.) | 0.1 | | Oral | 3 |
| Cotton (Sigmodon hispidus litteralis) | 0.1 | | Oral | 8 |
| Norway-wild (Rattus norvegicus) | 3.0 | | Oral | 3 |
| White-throated wood (Neotoma a. albigula) | <0.8 | | I.P. | 8 |
| Wood (Neotoma intermedia) | 1.5 | | Oral | 3 |
| Mice: | | | | |
| Deer mouse (Peromyscus sp.) | 4.0 | | Oral | 8 |
| House mouse (Mus musculus) | 8.0 | | Oral | 3 |
| Miscellaneous spp: | | | | |
| Meadow vole (Microtus pennsylvanicus) | 0.92 | | Oral | 9 |

TABLE 2--continued

| Species | $LD_{50}$* mg/kg | 95% Confidence Interval | Route of Administration | Reference |
|---|---|---|---|---|
| Nutria (Myocastor coypus) | 0.056 | | Oral | 9 |
| Porcupine (Erethizon dorsatum) | < 1.0 | | I.P. | 8 |
| Prairie Dog (Cynomys ludovicianus) | 0.3 | | Oral (S.T.) | 8 |
| Lagomorphs | | | | |
| Black-tailed jack rabbit (Lepus californicus) | 5.55 | | Oral | 9 |
| European Rabbit (Oryctolagus cuniculus) | < 0.8 | | Oral | 10 |
| BIRDS | | | | |
| Columbiformes | | | | |
| Domestic pigeon (Columba livia)(M-F) | 4.24 | 3.36-5.34 | Oral | 5 |
| Mourning Dove (Zenaidura macroura) (M-F) | 8.55-14.6 | | Oral (S.T.) | 5 |
| Anseriformes | | | | |
| Mallard (Anas p. platyrhynchos) | | | | |
| adult (M) | 10.0 | | Oral (S.T.) | 5 |
| adult (F) | 8.0 | | Oral (S.T.) | 5 |
| Pintail (Anas acuta tzitzihoa) | | | | |
| adult (M) | 10.0 | | Oral (S.T.) | 8 |
| adult (F) | 8.0 | | Oral (S.T.) | 8 |

TABLE 2--continued

| Species | $LD_{50}$* mg/kg | 95% Confidence Interval | Route of Administration | Reference |
|---|---|---|---|---|
| Galliformes | | | | |
| Chicken | 7.5 | | Oral | 3 |
| Chukar (Alectoris graeca) (M-F) | 3.51 | 2.58-4.78 | Oral | 5 |
| Gambels quail (Lophortyx gambeli) | 20 | | Oral | 3 |
| Japanese Quail (Coturnix coturnix japonica) (M) | 17.7 | 11.0-28.7 | Oral | |
| Ring-necked pheasant (Phasianus colchicus) (M) | 6.46 | 3.85-10.8 | Oral | 5 |
| Turkey (Maleagris gallopavo) (F) | 4.00 | 1.20-13.3 | Oral | 5 |
| Passerines | | | | |
| Brewer's blackbird (Euphagus cyanocephalus) | 2.0-3.0 | | Oral | 8 |
| English Sparrow (Passer domesticus) (M) | 3.00 | 2.38-3.78 | Oral | 5 |
| Magpie (Pica p. hudsonia) | 0.6-1.3 | | Oral | 8 |
| Raptors and Scavengers | | | | |
| Golden eagle (Aquila chrysaetos canadensis) | 1.25-5.00 | | Oral | 5 |
| American rough-legged hawk (Buteo lagopus sancti-johannis) | ~10.0*** | | Oral | 8 |

TABLE 2--continued

| Species | $LD_{50}$* mg/kg | 95% Confidence Interval | Route of Administration | Reference |
|---|---|---|---|---|
| Ferruginous rough-legged hawk (Buteo regalis) | ~10.0*** | | Oral | 8 |
| Marsh hawk (Circus cyaneus hudsonius) | ~10.0*** | | Oral | 8 |
| Great Horned Owl (Bubo virginianus pallescens) | ~10.0*** | | Oral | 8 |
| Black vulture (Coragyps atratus) | 15.0 | | Oral | 8 |
| Turkey vulture (Cathartes aura) | <20.0 | | Oral (S.T.) | 8 |
| AMPHIBIANS | | | | |
| Bull Frog (Rana catesbeiana) (M) | 54.4 | 25.6-115 | Oral | 5 |
| Leopard Frog (Rana pipiens) | 150.0 | | S.C. | 3 |
| South African Clawed toad (Xenopis laevis) | >500.0 | | I.P.<br>S.C. | 3 |



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FOOTNOTES TO TABLE 2:

1. Kaye (1970)
2. Arena (1970)
3. Chenoweth (1949)
4. Robison (1970)
5. Tucker and Crabtree (1970)
6. Jensen *et al*. (1948)
7. Robinson (1953)
8. Ward and Spencer (1947)
9. Denver Wildlife Research Center (Unpublished)
10. Lazarus (1956)

* Where confidence limits are not provided the figure is assumed to be an observed non-statistical estimate.

** Research has shown much variation between strains of laboratory rodents (Chenoweth, 1949).

*** Vomiting characteristic and early symptom.

M Male

F Female

I.V. Intravenous

I.M. Intramuscular

I.P. Intraperitoneal

S.T. Stomach Tube

S.C. Subcutaneous

< Less than

> Greater than

~ Approximately

TABLE 3: $LD_{50}$, average weight, and amount of properly treated coyote bait (1.6 g. of 1080/45.4 kg. of bait material) that selected species must consume in order to obtain a median lethal dose.

| Species | $LD_{50}$ mg/kg | Average Weight lbs. | Amount of Properly Treated Coyote Bait Containing $LD_{50}$ ozs. |
|---|---|---|---|
| Coyote | 0.1 | 30 | 1.4 |
| Cat (Domestic) | 0.2 | 3 | 0.3 |
| Fox | < 0.3 | 12 | < 1.6 |
| Bobcat | < 0.66 | 22 | < 6.6 |
| Bear | 0.5-1.0 | 300 | 68.0-136.0 |
| Mink | ~ 1.0 | 3 | ~ 1.4 |
| Marten | ~ 1.0 | 3 | ~ 1.4 |
| Magpie | 0.6-1.3 | 0.5 | 0.1-0.3 |
| Badger | 1.0-1.5 | 19 | 8.0-13.0 |
| Man | 0.7-2.1 | 150 | 47.6-142.8 |
| Golden Eagle | 1.25-5.0 | 7 | 4.0-15.9 |
| Hawks | ~ 10.0 | 2.5 | ~ 11.3 |
| Great Horned Owl | ~ 10.0 | 3.5 | ~ 15.8 |
| Black Vulture | 15.0 | 5 | 34.0 |
| Turkey Vulture | < 20.0 | 6 | < 54.0 |

## LATENT PERIOD

Sodium monofluoroacetate poisoning is characterized by a long and essentially irreducible latent period following the administration of the compound via any route. The period is seldom less than two hours, and is frequently greater (Pattison, 1959). Even a massive dose (50 times the $LD_{95}$) does not elicit immediate responses, although the latent period is reduced somewhat (Chenoweth, 1949). The latent period is related to sodium monofluoroacetate's biochemical mode of action. Specifically, it is the result of: (a) the time required for hydrolysis to monofluoroacetic acid, translocation, and cell penetration; (b) the time required for biochemical synthesis of a lethal quantity of fluorocitrate; and (c) the time required for the fluorocitrate to disrupt intracellular functions on a large enough scale to induce gross symptoms (Pattison, 1959). Variability in the length of the latent period among different species is directly related to differences of biochemistry.

## DETOXIFICATION AND EXCRETION

Gal *et al.* (1961) showed that rats (a) can metabolize sodium monofluoroacetate to non-toxic metabolites, and (b) can excrete monofluoroacetate as well as its toxic metabolite fluorocitrate. They also showed that when an animal obtains only a minimum lethal dose the possibility of secondary poisoning is reduced considerably.

Rats administered sodium monofluoro-2-$^{14}$C-acetate at rates varying from 1.77 mg/kg to 9.13 mg/kg completely metabolized a small percentage of the dose (i.e. evolved $^{14}CO_2$). Approximately 2 percent of the radioactivity appeared as $^{14}CO_2$ within 4 hours, irrespective of the amount of sodium monofluoro-2-$^{14}$C-acetate administered. No significant increase in the amount of $^{14}CO_2$ occurred after this period.

Analysis of the urine from the rats administered sodium monofluoro-2-$^{14}$C-acetate at the rate of 5.00 mg/kg revealed additional non-toxic metabolites. In all, seven radioactive compounds, two only in trace amounts, were found in the urine. Monofluoroacetate constituted only 13 percent of this urinary radioactive material, fluorocitrate only 11 percent, and an unidentified toxic metabolite 3 percent. Two non-toxic metabolites constituted 73 percent of the urinary radioactivity. Toxicity was determined by incubation with aconitase.

Rats administered sodium monofluoro-2-$^{14}$C-acetate at a rate of 1.77 mg/kg excreted approximately 32 percent of the radioactivity through the urine within 4 days (Table 4). Although these rats did exhibit symptoms of monofluoroacetate poisoning, none died during the 4-day period. The peak rate of excretion occurred during the first day and then gradually decreased so that by the fifth day the rate of excretion was less than

0.3 percent. Rats administered sodium monofluoro-2-$^{14}$C-acetate at a rate of 5.00 mg/kg excreted up to 32 percent of the radioactivity through the urine prior to death (Table 4); all died within 2 days. The peak rate of excretion occurred during the first day and dropped sharply thereafter. Rats administered sodium monofluoro-2-$^{14}$C-acetate at a rate of 10.53 mg/kg excreted only 0.5 percent of the radioactivity through the urine prior to death; all died within 4 hours.

Research indicates that dogs (Foss, 1948) and rabbits (Rowley, 1963) also have the ability to metabolize monofluoroacetate compounds to non-toxic metabolites and/or excrete monofluoroacetate compounds and fluoro-citrate. To a greater or lesser degree probably all animals share this ability.

TABLE 4: Recovery of radioactivity from the urine of rats administered sodium monofluoro-2-$^{14}$C-acetate (Gal et al., 1961).

| Dose | 1.77mg/kg | 5.00 mg/kg |
|---|---|---|
| Time (Hours) | Percent of dose recovered | Percent of dose recovered |
| 4 | 0.5 | 3.0 |
| 24 | 14.1 | 25.5 |
| 48 | 10.1 | 3.9 |
| 72 | 6.5 | --- |
| 96 | 0.3 | --- |
| Total | 31.5 | 32.4 |

## TOLERANCE AND ACCUMULATION

Repeated sub-lethal doses of monofluoroacetate have increase the tolerance of some species to subsequent challenging doses. Golden eagles (Denver Wildlife Research Center, unpublished data), rats (Foss, 1948; Kandel and Chenoweth, 1952; Miller and Phillips, 1955), mice (Quin and Clark, 1947), and possibly rhesus monkeys (Chenoweth, 1949) have exhibited this response; however, dogs have not (Foss, 1948). The resistance extends only partially to slightly higher challenging doses, and the ratio of doses cannot be extended (Chenoweth, 1949). Conversely, repeated sub-lethal doses of monofluoroacetate have accumulated in other species until they reached lethal levels. Dogs, guinea pigs, (Foss, 1948), rabbits (Steyn, 1934; Rowley, 1963), and mallards (Tucker and Crabtree, 1970), have exhibited this response; however neither mice (Quin and Clark, 1947), nor rats (Foss, 1948) have exhibited it.

Tolerance is a time-related phenomenon. Chenoweth (1949) pointed out that rats administered a 0.5 mg/kg dose of monofluoroacetate became largely resistant to the effects of a 5.0 mg/kg dose of monofluoroacetate within more than 4 hours and less than 24 hours, the resistance lasting about 48 hours. Kandel and Chenoweth (1952) pointed out that rats administered a 1.0 mg/kg dose of monofluoroacetate became largely resistant to the effects of a 6.0 mg/kg dose when administered 28 hours later, but not when administered only 14 hours later. A sub-lethal dose administered 24 hours prior to a challenging dose, not only reduced overall mortality, but also lengthened the period between administration of the challenging dose and death in those animals which did succumb.

Cumulation is also a time-related phenomenon. Foss (1948) reported that a dog administered monofluoroacetate at a rate of 0.025 mg/kg daily was unaffected until the fifth dose, when convulsions and death occurred; however, larger sub-convulsive doses could be administered to dogs on alternate days or less frequently without the dogs succumbing. In a 16-day test more than half of the rabbits (Oryctolagus cuniculus) survived daily doses of 0.175 mg/kg, but only 37 percent survived this amount if given at 12-hour intervals (Rowley, 1963). The two test populations stabilized at these percents of survival 9 or 10 days into the 16 day experiment.

Mazzanti, et al. (1965), working with albino rats, showed that continued sub-lethal doses of sodium monofluoroacetate, like continued sub-lethal doses of fluoroacetamide, caused regressive changes in the germinal epithelium of the seminiferous tubules. Sodium monofluoroacetate was administered intraperitoneally in 9 doses of 2.5 mg/kg each during 11 days. The intermediate stages of spermatogenesis (spermatids and spermatocytes) were the first to be damaged, but subsequently the initial stage of spermatogenesis (spermatogonia) was also damaged. By the eleventh day no stages of the seminal line were present in the seminiferous tubules. Mazzanti, et al. (1968), again working with albino rats, showed that the germinal epithelium of the seminiferous tubules regenerated after treatment with sub-lethal doses of fluoroacetamide was halted; regeneration was complete within 165 days. Similar results are expected with sodium monofluoroacetate, since it and fluoroacetamide act in the same manner.

## SECONDARY POISONING

Secondary poisoning can occur with sodium monofluoroacetate. However, Gal et al. (1961) have shown that rats can metabolize sodium monofluoroacetate to non-toxic metabolites and/or excrete a large amount of sodium monofluoroacetate and fluorocitrate prior to death, if the dose is approximately an $LD_{50}$ (up to 32 percent of a 5.00 mg/kg dose of sodium monofluoroacetate excreted). In addition, sodium monofluoroacetate tends to exert an emetic action, especially on canids which have ingested more than an $LD_{50}$; thus, a portion of the toxic material may be regurgitated

(Robinson, 1949, Denver Research Center, unpublished data). These features can result in a portion of the poison ingested by an animal not being present in the animal at death. In any event, due to dilution, the concentration of sodium monofluoroacetate in the body of the victim will be much less than in the bait itself. Therefore, an animal feeding on a sodium monofluoroacetate victim is much less likely to receive a lethal dose than from feeding on the treated bait itself, even if the animal feeds on the internal organs and their contents, the portions of the victim with the highest concentration of sodium monofluoroacetate and/or its toxic and non-toxic metabolites.

The golden eagle, an animal that normally consumes the internal organs before other portions of its food, demonstrates the reduced hazard of acute poisoning via secondary sources. To obtain an $LD_{50}$ (1.25-5.00 mg/kg) of sodium monofluoroacetate from a secondary source such as coyotes, a 7-pound golden eagle would have to consume the internal organs of from 7 to 30 coyotes killed by sodium monofluoroacetate--assuming the coyotes ingest an $LD_{50}$ (0.1 mg/kg) and do not excrete, detoxify, or regurgitate any of the toxicant and that as in rats approximately 40 percent of the dose is present in the internal organs at death.[10] The internal organs of a coyote account for approximately 20 to 25 percent of its live weight, or 6 to 7 pounds. A golden eagle's daily consumption of food equals approximately 30 percent of its live weight, or 2 pounds (Denver Wildlife Research Center, unpublished data). As noted previously, animals can metabolize and/or excrete continued small doses of sodium monofluoroacetate without succumbing (Foss, 1948).

Since regurgitated material is actually only partially digested bait it presents a possibility of primary poisoning. This vomitus, however, is quite finely divided in comparison to the 1080 stations, a condition which speeds the decomposition of the vomitus and speeds the leaching of the sodium monofluoroacetate from the vomitus into the soil (Staples, 1968).

## TREATMENT OF SODIUM MONOFLUOROACETATE POISONING

There is no highly effective antidote for sodium monofluoroacetate; medical treatment is mainly symptomatic. First aid treatment consists of immediate emesis and gastric lavage followed by an oral dose of magnesium or sodium sulfate to remove the poison from the alimentary tract before absorption of lethal quantities can occur. The patient should be kept quiet and barbiturates administered to control convulsions. Monoacetin (glyceryl monoacetate), acetamide, as well as a combination of sodium

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[10] The amount of material that an eagle would have to consume to obtain an $LD_{50}$ of course depends upon the amount of bait the coyotes consume.

acetate and ethanol have shown antidotal effects in animals including monkeys. No report of their use in humans has appeared in the literature. The recommended dose for humans of monoacetin is 0.5 mg/kg of undiluted monoacetin intramuscularly every half hour for several hours and then at a reduced level for at least 12 hours. The site of intramuscular injection must be varied because of local pain and edema. If intramuscular administration is not feasible, a mixture of 100 ml. of undiluted monoacetin in 500 ml. of water can be given orally and repeated in an hour. If monoacetin is not available, acetamide or a combination of sodium acetate and ethanol may be given in the same dose. Intravenous administration of procainamide also has shown antidotal effects (restoration of normal rhythm in ventricular fibrillations). (Gleason et al. 1969; Arena, 1970).

## TRANSLOCATION AND PERSISTENCE IN SOIL

Hilton et al. (1969) noted that salts of monofluoroacetic acid exhibit a high degree of adsorption to root tissues as well as other cellulosic materials; therefore, any sodium monofluoroacetate which is leached from baits is not likely to be carried far by the leaching water, but to be held in the upper soil layers. Saito et al. (1966) analyzed water from streams in a sodium monofluoroacetate-treated area for 5 months following the application of sodium monofluoroacetate rodent bait and did not detect a trace of the chemical.

Horiuchi (1960) demonstrated that fluoroacetamide breaks down in the soil. David and Gardiner (1966) demonstrated that both sodium monofluoroacetate and fluoroacetamide break down in the soil, and concluded that there are no apparent reasons for condemning the use of these compounds because of a buildup of toxic residues in the soil. Sodium monofluoroacetate either exhibited no measurable toxicity at all or exhibited no measurable toxicity within 2 weeks, depending upon the soil type, when applied to soils at 10 ppm; and exhibited no measurable toxicity within 11 weeks when applied to soils at 50 ppm (Table 5).[11]

Actually, the results of Horiuchi (1960) and David and Gardiner (1966) are not entirely unexpected. It seems likely that naturally occurring decomposer organisms capable of degrading the monofluoroacetate ion ($FCH_2COO^-$) should exist since several toxic plants normally synthesize monofluoroacetic acid, and others can synthesize it under certain conditions. Indeed, soil bacteria which can decompose monofluoroacetates by cleaving the carbon-fluorine bond to yield fluoride ions and glycolate ($HOCH_2COO^-$) have been isolated in Japan (Horiuchi, 1961; Tonomura et al., 1965), in England (Kelly, 1965), and in the United States (Goldman, 1965).

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[11] The soil samples were in 1-pound screw top jars; therefore, the toxicants were not leached out of the soil samples.

TABLE 5: Results of bioassay using *Aphis fabae* on broad beans to test for residues of sodium monofluoroacetate and fluoroacetamide in two soils (David and Gardiner, 1966).

| Dose applied to the soil (ppm) | Type of soil | Result of biological test for toxic residues after weeks | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 0 | 1 | 2 | 3 | 5 | 9 | 11 | 12 | 17 |
| | | Sodium Fluoroacetate | | | | | | | | |
| 10 | Kettering loam | - | - | - | - | | | | | |
| | Garden soil | ++ | ++ | - | - | | | | | |
| | Garden soil sterilized | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| 50 | Kettering loam | ++ | ++ | ++ | ++ | ++ | + | - | - | - |
| | Garden soil | ++ | ++ | ++ | ++ | ++ | + | - | - | - |
| | Garden soil sterilized | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| | | Fluoroacetamide | | | | | | | | |
| 10 | Kettering loam | - | - | - | - | | | | | |
| | Garden soil | ++ | ++ | + | - | - | - | | | |
| | Garden soil sterilized | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ |
| 50 | Kettering loam | ++ | ++ | ++ | ++ | ++ | + | - | - | - |
| | Garden soil | ++ | ++ | ++ | ++ | ++ | + | - | - | - |
| | Garden soil sterilized | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ | ++ |

++ Aphid population entirely eliminated in less than 5 days (high residue).

\+ Aphid population reduced but not eliminated (some residue).

\- No noticeable effect on aphid population (residue below level detectable).

The bacteria appear to be Pseudomonas species and are able to cleave the carbon-fluorine bond only adaptively. Tonomura et al. (1965) and Goldman (1965) noted that when grown in media containing sodium monofluoroacetate as the sole source of carbon, an enzyme extract of the bacteria catalyzes the defluorination of monofluoroacetate. However, when grown in media containing more easily metabolized substrates, such as succinate, glycolate or acetate, as the sole source of carbon, an enzyme extract of the bacteria does not catalyze the defluorination of sodium monofluoroacetate (Table 6). Growth of Pseudomonas species in media containing sodium monofluoroacetate or fluoroacetamide as the sole carbon source is only 15 percent as rapid as growth in media containing easily metabolized substrates (Kelly, 1965).

TABLE 6: Effect of the carbon source on growth and on the carbon-fluorine bond cleaving ability of enzyme extracts from defluorinating bacteria (Tonomura et al., 1965).

| Carbon Source | Growth* | Specific carbon-fluorine bond cleaving ability of enzyme extract |
|---|---|---|
| Glucose (0.5%) | 0.975 | 0 |
| Sodium monofluoro-acetate + Yeast extract (each 0.25%) | 0.610 | 0.63 |
| Sodium monofluoroacetate (0.5%) | 0.128 | 16.3 |

* Bacteria were aerobically grown for 16 hours. Growth is expressed with an optical density at 430 mμ.

The enzyme responsible for the carbon-fluorine bond cleavage in monofluoroacetates is specific to that function. Only a small amount of halides are released from other monohalide acetates (Cl, Br, I).

Goldman (1965) proposed a two-step thioether mechanism for the enzymatic defluorination of monofluoroacetates. The first step is rate limiting. The $OH^-$ in the second step is derived from water. There is no evidence that this defluorination is reversible (Goldman and Milne, 1966).

$$Enz\text{-}S^- + XCH_2COO^- \rightarrow Enz\text{-}S\text{-}CH_2COO^- + X^-$$

$$Enz\text{-}S\text{-}CH_2COO^- + OH^- \rightarrow HOCH_2COO^- + Enz\text{-}S^-$$

## TRANSLOCATION AND PERSISTENCE IN PLANTS

Sodium monofluoroacetate which leaches into the soil may be absorbed by plants before bacterial defluorination occurs. Hilton et al. (1969) noted that between 5 and 10 percent of the radioactivity removed from a solution of ammonium monofluoro-2-$^{14}$C-acetate by sugar cane is translocated upward to the leaves; the rest remains adsorbed on the roots. Monofluoroacetate can also be absorbed through the leaves of plant (David and Gardiner, 1951; Hilton et al., 1969). These investigators did not determine whether the compound underwent metabolic alterations once absorbed.

Preuss et al. (1968) and Ward and Haskisson (1969) provided indirect evidence (evolvement of $^{14}CO_2$ by plants incubated with sodium monofluoro-2-$^{14}$C-acetate) that plants can decompose sodium monofluoroacetate.

Preuss and Weinstein (1969) proved that plants contain an enzyme which decomposes monofluoroacetates by cleaving the carbon-fluorine bond. About 15 percent of the fluoride supplied as sodium monofluoroacetate to germinating peanut seeds, Archis hypogeae, L., was found in the inorganic form in the seedling or in the incubating media after 48 hours (Table 7).[12] In controls containing killed seeds or no seeds at all only between 2 and 5 percent of the fluoride supplied as sodium monofluoroacetate was found in the inorganic form after 48 hours of incubation.[13] In germinating seeds 29 percent of the fluoride was in the inorganic form after 48 hours of incubation with sodium monofluoroacetate, while in killed seeds all the fluoride was still in the organic form after 48 hours of incubation with sodium monofluoroacetate.

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[12] A more rapid process of defluorination could actually be maladaptive since inorganic fluoride is considerably more toxic to plants than is monofluoroacetate (Preuss and Weinstein, 1969).

[13] This demonstrates decomposition of sodium monofluoroacetate in aqueous solutions.

TABLE 7: Distribution of inorganic fluoride between germinating and boiled peanut seeds and buffer solution supplied with different sources of fluorine for 48 hours (Preuss and Weinstein, 1969).

| Treatment | | | Inorganic fluoride found | | Inorganic fluoride as percent of total | |
|---|---|---|---|---|---|---|
| Type of seeds | Source of fluoride | Total fluoride added μg | In Incubation liquid μg | In seeds μg | In incubation liquid | In seeds |
| Germinating | NaF | 80 | 36 | 45 | 45 | 56.3 |
| Germinating | $FCH_2COONa$ | 244 | 11 | 23 | 4.5+0.8 | 10.3+2.1 |
| Boiled | $FCH_2COONa$ | 244 | 4 | 0 | 1.7+0.9 | 0 |
| None | $FCH_2COONa$ | 244 | 11 | - | 4.6+1.0 | - |
| None | None | 0 | 0 | - | 0 | - |

## USE OF SODIUM MONOFLUOROACETATE IN THE UNITED STATES

The use of sodium monofluoroacetate in the United States is rigidly regulated. Sodium monofluoroacetate is not available to the general public. The chemical is registered under the Federal Insecticide, Fungicide and Rodenticide Act (61 Stat. 163; 7 U.S.C. 135-135k) for use only by governmental agencies and experienced pest control operators for the control of coyotes, gophers, ground squirrels, prairie dogs, field mice, and commensal rodents. Only the Bureau of Sport Fisheries and Wildlife has a registration under this Act to use sodium monofluoroacetate for coyote control.

The two United States manufacturers of sodium monofluoroacetate, Tull Chemical Company, Inc., and Fike Chemicals, Inc., require the following (in writing) prior to sale:

1. The purchaser agrees to assume full responsibility for the use of the chemical, and, except the Bureau of Sport Fisheries and Wildlife, to use the chemical only for rodent control.

2. The purchaser must be covered by public liability insurance for exterminator operations of $50,000 to $100,000; and provide the name of the insurance company providing said coverage, the number of said insurance policy, and the expiration date of said insurance policy.

3. The purchaser agrees that the sodium monofluoroacetate purchased will not be given away or resold in any form.

4. The purchaser agrees that the sodium monofluoroacetate will be used only by personnel experienced in and familiar with the dangers and use of poison, and instructed in the use of sodium monofluoroacetate.

5. The purchaser agrees to deliver to the manufacturers for disposal any sodium monofluoroacetate in his possession, if the required liability insurance is terminated for any reason, or if his use of sodium monofluoroacetate is discontinued.

Total sales by these manufacturers over the past three years have averaged approximately 2,600 pounds annually. Sales to private pest control operators account for approximately 50 percent; sales to city, county, and State governments approximately 20 percent; sales to Federal agencies approximately 12 percent; and export sales approximately 18 percent.

In 25 years of use in the United States there have been 4 suicidal deaths and 12 accidental deaths definitely involving sodium monofluoroacetate, and 4 accidental deaths possibly involving sodium monofluoroacetate (Bureau of Sport Fisheries and Wildlife, unpublished data). One of the accidental fatalities was connected with Bureau use of sodium monofluoroacetate to control commensal rodents. The accident occurred in 1949; the person requesting control failed to prevent access to the treated building by children, contrary to Bureau instructions.

## USE OF SODIUM MONOFLUOROACETATE BY THE BUREAU OF SPORT FISHERIES AND WILDLIFE

Sodium monofluoroacetate procured by the Bureau of Sport Fisheries and Wildlife is used only by or under the direct supervision of Bureau personnel trained in such use, unless specifically excepted in writing by either a Regional Director or the Bureau Director (Bureau of Sport Fisheries and Wildlife, 1970). Regional Directors may approve a sale or transfer of prepared rodent bait material only to cities, counties, States, or other agencies of the Federal Government, except the Department of Defense, provided the recipient:

a. Assumes full responsibility and furnishes evidence of technical competence for its independent use of the bait material;

b. agrees to restrict use of the bait to its direct supervision in the manner and for the purpose for which procured; and

c. agrees not to sell, transfer, or give the bait to any other agency or persons.

The sale or transfer of 1080 bait to the Department of Defense requires the approval of the Bureau Director, and the approval of the Armed Forces Pest Control Review Board.

The Bureau reserves the right to refuse to undertake requested animal damage control when--in its judgement--control is not justified, would endanger a native species, would pose a threat to the environment, or would not be in accord with the National Environmental Policy Act of 1969 (PL 91-190, 83 Stat; 852-856). Therefore, any animal damage control work the Bureau does undertake with sodium monofluoroacetate must be conducted in a manner which minimizes the hazards to non-target species.

When sodium monofluoroacetate is used in coyote damage control operations the bait material, an eviscerated carcass or portion of a carcass of a domestic or non-game animal averaging 50 to 100 pounds, is treated at a rate of 1.6 grams of sodium monofluoroacetate per 100 pounds of bait material (35 ppm). Treatment is made at this low concentration for the sake of selectivity.

This low concentration reduces the hazards to carnivorous non-target species, both avian and mammalian, which are more tolerant to sodium monofluoroacetate (Table 2). First, the low concentration of sodium monofluoroacetate in the bait decreases the possibility of non-target species obtaining lethal doses from the bait. Second, the low concentration of sodium monofluoroacetate in the bait decreases the possibility of non-target species obtaining lethal doses from secondary sources. It is recognized that in spite of these characteristics of the treated bait, additional measures are necessary to increase the margin of safety and assure maximum protection of non-target species.

Baits are placed at established crossings and driftways having maximum use by coyotes in habitat having minimum use by most non-target carnivorous species. This practice, in conjunction with the Bureau policy of low density bait placement (normally no more than one per township) and the much smaller home ranges of most non-target carnivorous mammals, precludes a large percentage of the populations of these non-targets from even encountering the baits. Continuing studies indicate that populations of non-target carnivorous species have not measurably decreased in the vicinity of Bureau control operations in the past 30 years (Denver Wildlife Research Center, unpublished data).

Baits are placed as late in the fall as practicable, in keeping with effectiveness in controlling damage, and conditions of weather and travel. Baits are removed as early in the spring as weather and travel conditions will permit after allowing a suitable, but minimum time of exposure. To assure recovery, baits are securely fastened to immovable objects when

set out in the fall and the location is described in writing--at least two persons must have firsthand knowledge of each location. Baits are disposed of by burning and burying or by deep burial.

To protect domestic animals and man, baits are placed only after written agreements are signed with the landowner, lessee, or land administrator requesting coyote damage control, and the baits are placed only in sparsely inhabited areas not generally used by the public during the period of bait exposure. Area residents are notified of the placement, and appropriate warning signs are posted on roads and trails leading to the bait site, at the site, and at other locations deemed necessary.

Grain bait for rodent damage control is treated at a rated of 2 or 10 ounces of sodium monofluoroacetate per 100 pounds of grain depending upon planned use. The secondary hazard to most carnivorous species is minimized because the toxicology of sodium monofluoroacetate often results in the rodent dying in its underground burrow. As an additional safeguard, the grain bait is dyed a yellow color which reduces its acceptability to seed-eating birds. As always, no control is conducted until written agreements are signed with the landowner, lessee, or land administrator requesting the control. Area residents are advised of the hazard to domestic animals of these field rodent damage control operations.

The Bureau's use of sodium monofluoroacetate resulted in but 37 known incidents of domestic animal poisoning from 1959 through 1969. No human fatalities have ever resulted from Bureau use of sodium monofluoroacetate to control coyote and field rodent damage.

## SUMMARY

Monofluoroacetic acid is biosynthesized by several toxic plants, and can be biosynthesized by other plants in the presence of high levels of inorganic fluoride.

Sodium monofluoroacetate is an almost tasteless, white, powdery, hygroscopic fluoro-organic salt. It is very soluble in water, but relatively insoluble in organic solvents. It has a relatively high degree of stability; however, it is unstable above 110 degrees centigrade and decomposes at 200 degrees centigrade, yielding approximately 20 percent hydrogen fluoride by weight. In addition, it decomposes slowly in aqueous solutions.

Sodium monofluoroacetate may be absorbed through the gastrointestinal tract, open wounds, mucous membranes, and pulmonary epithelium. It is not readily absorbed through intact skin. Except for dermal administration the toxicity of sodium monofluoroacetate is not modified by the mode of administration. With large lethal doses (approximately 2 x $LD_{50}$), approximately 40 percent of the amount administered is found in the internal organs at death either as monofluoroacetate, or as a toxic or non-toxic metabolite.

In the body sodium monofluoroacetate, like other monofluoroacetates, is metabolized to highly toxic fluorocitrate. Fluorocitrate blocks the Krebs cycle, the major mechanism for releasing energy from food. The resulting buildup of citrate blocks glucose metabolism, another mechanism for releasing energy from food. The blockage of these processes causes the energy supply to be reduced to a point where cellular permeability barriers are destroyed, resulting in loss of function and finally cellular death. Eventually gross organ or organ system disorders are manifested. Deaths results from cardiac and/or central nervous system failure.

Animals can metabolize sodium monofluoroacetate to non-toxic metabolites and can excrete monofluoroacetate as well as its toxic metabolite fluorocitrate. Tests with rats administered 5.00 mg/kg of sodium monofluoroacetate show that they excreted in the urine up to 32 percent of the amount prior to death, with non-toxic metabolites constituting 73 percent of the amount excreted.

Sub-lethal doses of sodium monofluoroacetate have led to a tolerance to subsequent challenging doses in certain animals. In others, repeated sub-lethal doses of sodium monofluoroacetate have led to an accumulation of lethal quantities. Both phenomena are time related. Repeated sub-lethal doses have also led to reversible damage to the epithelium of the seminiferous tubules.

It is generally agreed that secondary poisoning can be demonstrated with sodium monofluoroacetate. However, simple dilution and the fact that animals can metabolize to non-toxic metabolites and/or excrete a large quantity of a dose prior to death--if the dose is approximately an $LD_{50}$--reduces the hazard of acute poisoning via secondary sources considerably.

As an example of the reduced hazard of acute poisoning via secondary sources, a 7-pound golden eagle would have to consume the internal organs of from 7 to 30 coyotes killed by sodium monofluoroacetate to receive a median lethal dose (1.25 to 5.00 mg/kg)--assuming the coyotes ingest an $LD_{50}$ (0.1 mg/kg) and do not excrete, detoxify, or regurgitate any of the toxicant and that as in rats approximately 40 percent of the dose is present in the internal organs at death.

Since sodium monofluoroacetate acts as an emetic, especially on canids, there is danger of primary poisoning from eating the vomitus. Even canids, however, do not always regurgitate a portion of the undigested bait, especially if only an $LD_{50}$ is ingested.

There is no highly effective antidote for monofluoroacetate poisoning; medical treatment is mainly symptomatic. However, monoacetin, acetamide, sodium acetate and ethanol, and procainamide have shown antidotal effects in some animals.

Salts of monofluoroacetic acid exhibit a high degree of adsorption to root tissues and other cellulosic materials, and are decomposed adaptively by soil bacertia, apparently of the genus Pseudomonas. Therefore, any sodium monofluoroacetate leached into the soil will likely be held in the upper layers rich in microorganisms and be decomposed by bacteria. In tests conducted in England the compound either exhibited no measurable toxicity from the start or exhibited no measurable toxicity within 2 weeks, depending upon the soil type, when applied to soils at 10 ppm; and exhibited no measurable toxicity within 11 weeks when applied to soils at 50 ppm. The Bureau of Sport Fisheries and Wildlife treats coyote baits at 35 ppm, and the concentration of sodium monofluoroacetate in the surrounding soil caused by leaching from the bait would be much less.

Sodium monofluoroacetate which leaches into the soil may be taken up by plants. However, only a small percent is translocated upward to the leaves--the rest remains adsorbed on the roots. Plants can decompose the compound. In one experiment, after 48 hours of incubation with sodium monofluoroacetate, plants had decomposed 29 percent of the absorded sodium monofluoroacetate.

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